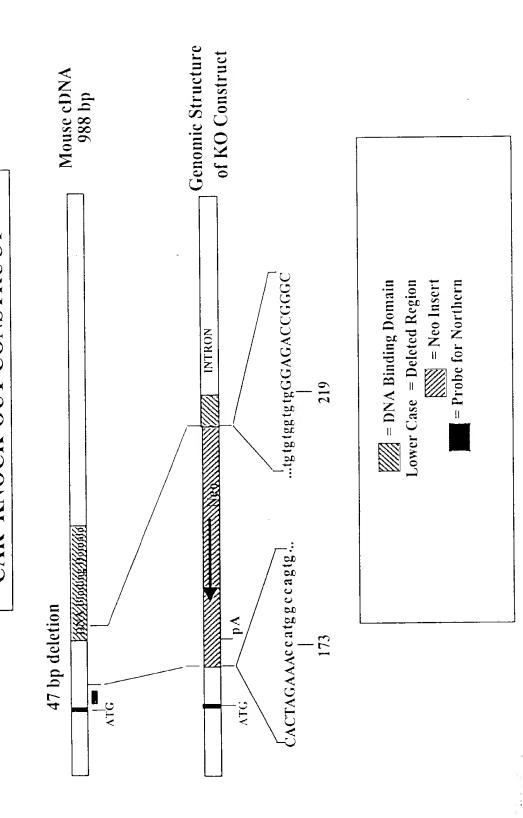
Figure 1

## CAR KNOCK-OUT CONSTRUCT



## FIGURE 2

Section A.

.....aaaatttacccaacatagatttatctaatgtaattcctatctgcagaacatccaaatactttggaaattatttnttgtggttgtagctgtttgaatauttattagaatauttagaatagaatauttagaatagg cag tgg tgg caeacacctt ta atcccag cacttgg gag gcag ag gcag tgg a attat gag ttt gag gccag cct gg tctacag ag tgg and the same statement of the same statgtgatgtttatcacaatagaaagc.....

## Section B.

.....a a a gagg to a teaggett gg cag caa g t geet t t geet a ceg a g tett t a cae cag et cea ceg t gg t t t t gag a cag te t cea ceg g get t t t gag a cag te t cea ceg g g te t t t gag a cag te t cea ceg g g te t t t g cae cag te t t t t g cae cag te t t g cae cag te t t g cae cag te t t t g cae cag te t t g cae cag te t t t g cae cag te t t t g cae cag te t t g cae cag te t t g cae cag te tactgg atttcag caa agaa agctagg ctt gccttctt gtctctgcctcctt gg cattgg aattat gagtt gttccaccgt gccatttttaa aaa atgtagg ag tagged gagtagg aggaattat gagtt gttccaccgt gccatttttaa aaa atgtagg ag tagged gagtagg aggaattat gagtt gttccaccgt gccatttttaa aaa atgtagg ag tagged gagtagg ag tagg ag tagged gagtagg ag tagged gagtagg ag tagg agggttctaggaattaaactcggctctcggtgcttatatagtgagtactttacagagggagtcaccttgccagcacctagaattcacttttattcatatctctcccattgtttcctggcttattcaggatccatgcaaaaaggggagtgtagatttagcctaaagctcacccacagggaaatcctccaggagt  $\verb|ccceaccccacaccccacacccagg| tettigecctgggtccagagtctgggtcctacctacatatggcaccgaggatacctagaggccccat|$ gaag agag accat teag gag accat teag gag accat teag gag accat TGACAGCTATGCTAACACTAGG account to the contract of the contract teag and the contract teag gag accat teag gag<u>GGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGAGGGCTGCAAGGGCTTCTTCA</u>  $\underline{Gg} tga atgette et cecea acaga aa caaccega cattte tate agtee accttta aa caetgg ta caectee aa gttata at cetett geagant acceptance of the contraction of the contra$ eta aget geaet gecea g t g teta g eact ctea at cit g et gacea ca a egeag t g a a a et g g t g a ceta at gacea g g t ta a e ca teta g et g a e consideration de la cottgtcccagagacagagcctaagagtcaagaacacttgtgtagcacacactacctgcaaagcaccgagatgattgccacacgagggttcct $gagtaacettgtgtteteatgaaaacgeteeaactacetetgaagacetttgageaeageteagatgagtetgttgttaaategatee\ldots \\$ 

## Section C.

..... t g catt g ctttctact g aagt g tatcaca g at gaat at gag at c g acag a aagt g t g cag g g at c c c c t g c cat ct g g aa a cactta at the state of the statea caggeacagegggcgggcagagaaagcatetttgcaactgaatcagcagcagaaagaactggtccagatectcctcggggcccacactcaagaaggctatgccctgatggaggaca

 $5\beta$ -Pregnan-3,20-dione is an hCAR Agonist

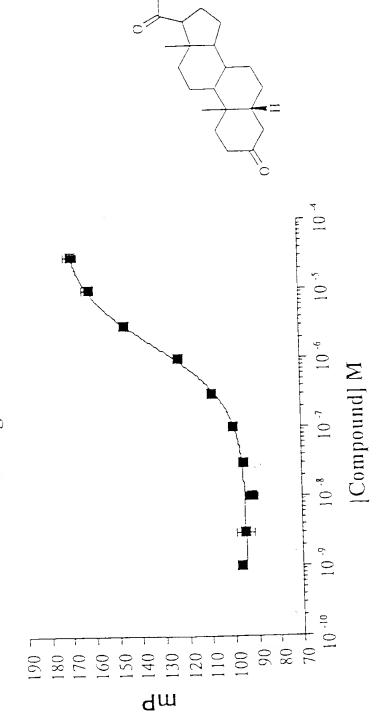


Figure 3

Androstanes are hCAR Antagonists

$$_{\rm C}$$
 S  $_{\rm C}$  -Androst-16-cn-3  $_{\rm C}$   $_{\rm C}$  -ol + 5  $_{\rm H}$  M 5  $_{\rm B}$ -Pregnan-3,20-dione

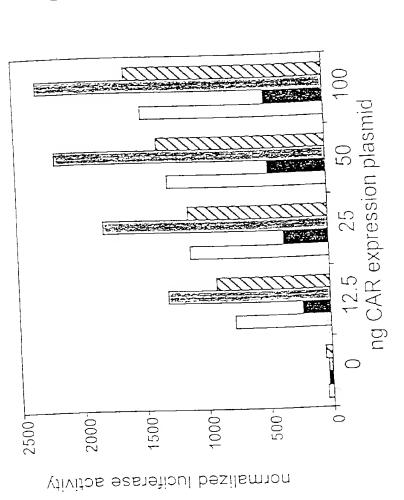
1.2 µM

$$5\,\alpha$$
-Androstan-3  $\alpha$ -ol +  $5\,\mu M$  5  $\beta$ -Pregnan-3,20-dione

$$5\alpha$$
-Androst-16-en-3  $\alpha$ -ol  $5\alpha$ -Androstan-3  $\alpha$ -ol

 $5\alpha$ -Androstan- $3\alpha$ -ol

 $5\alpha$ -Androst-16-en- $3\alpha$ -ol



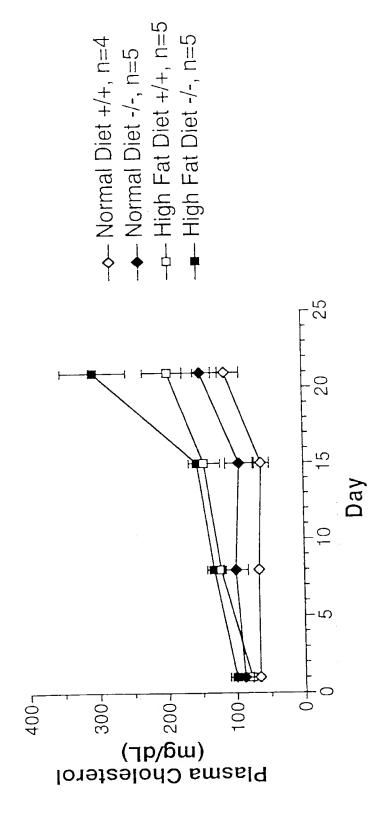
□ vehicle

5α-androstan-3α-ol

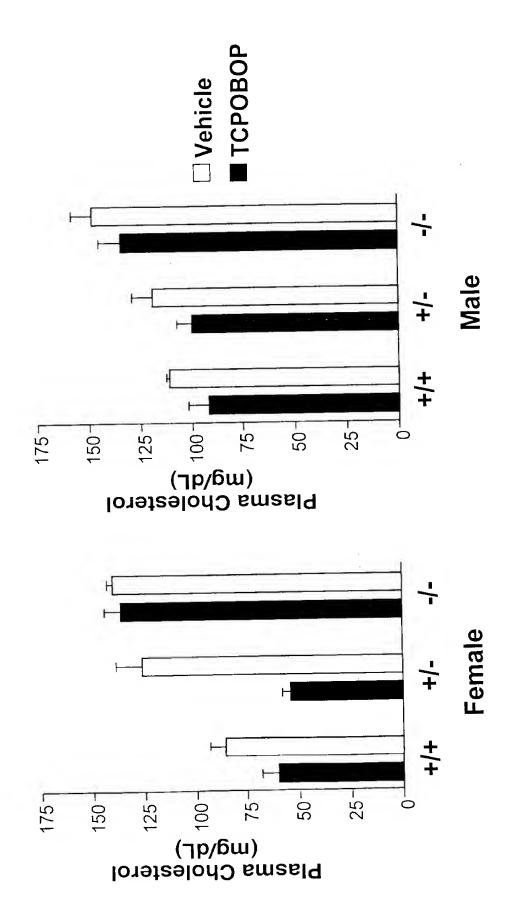
■ 5β-pregnan-3,20-dione

 $B 5\alpha$ -androstan- $3\alpha$ -ol

5β- pregnan-3,20-dione



High Fat diet = Picolab 5053 (containing 1.25% cholesterol and 10% fat) Normal diet = Picolab 5053 (containing 4% fat)



- LDL/VLDL - Origin ] HDL ₽ W から F M マイナナナ ≅ 🎖 SEX GENOTYPE Vehicle **Treated** 

π 8

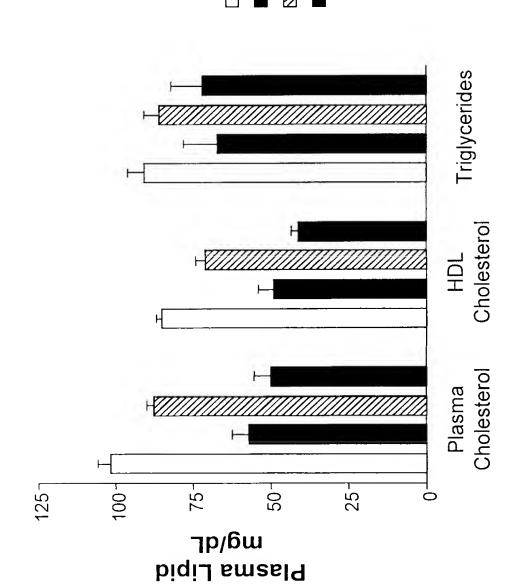
∑×

TCPOBOP Treated

- LDL/VLDL ] HDL

- Origin

₽ W FW π 8 ≥ %  $\mathbb{M} \bigvee$  $\mathbb{Z} \stackrel{\vdash}{\geqslant}$ SEX GENOTYPE



Male - Vehicle
Male - TCPOBOP
Female - Vehicle
Female - TCPOBOP